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Complimentary CLE Webinar

Updates on BAP1 and BRCA Genes

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Sponsored by: ToxicoGenomica

Webinar Overview

- First, I will comment on law and science developments

- Second, Dr. Len van Zyl will address key recent scientific studies, including:
  - his team's Nielsen 2025 study regarding BAP1
  - large scale studies further establishing that germline mutations cause many cancers
  - studies explaining the mechanisms involved in cancers caused by BRCA1 and 2

- Third, Michael Zapata will focus on acquiring and utilizing genomic data via, including:
  - genetic data in medical records
  - subpoenas to sequencing operations
    - commercial sequencing companies such as Invitae, Tempus, etc
    - hospitals with internal sequencing services

Law and Science Update

- Recent Developments
- Some Key Points/Reminders from Prior Webinars
  - Whole Genome Sequencing (WGS)
  - Stipulations and Orders for Extensive, Flexible Sequencing
  - Flexible Reporting of Sequencing Results Can Eliminate Inefficiencies and Disputes

New Roggli et al Article:

"Recent trends in the causation of peritoneal mesothelioma: fiber burden analysis of ten cases"

- Roggli VL, Novakovic S, Ghio AJ, Li H, Pina-Oviedo S, Carney JM, Sporn TA, Glass CH, Pavlisko EN. Recent trends in the causation of peritoneal mesothelioma: fiber burden analysis of ten cases. Ultrastruct Pathol. 2025 Mar 26:1-8.
  - https://pubmed.ncbi.nlm.nih.gov/40143456/

"We performed fiber burden analysis on lung tissue in 10 cases (six men, four women) of peritoneal mesothelioma since 2010."

More re New Roggli et al Article

- Key quotes from abstract:

- “The median age for the six men was 62 years (range: 53-75 years). Three cases were epithelioid type and three were biphasic. Two of six cases (33%) had an elevated lung fiber burden, with one case exclusively crocidolite and the other predominately amosite.

- The median age for the four women was 55 years (range: 39-63 years). Two cases were epithelioid type and two were biphasic. None of the four had an elevated lung fiber burden.

- Our findings are consistent with contemporary epidemiological studies indicating that a minority of peritoneal mesotheliomas occurring in men are asbestos related and very few are asbestos related in women.”

Mizer Update – WGS and Flexible Reporting Used

Reminder re Specifics of Mizer & Stipulation to WGS and Flexible Results Reporting

- Mizer is an ongoing New Jersey case; spring and summer 2024 orders from Judge Viscomi essentially Mizer up as a test case for NJ regarding genetic testing in asbestos cases

- Moving defendants filed an extensive brief and supporting declarations on July 30, 2024
  - Declarations by Len van Zyl, Ph.D, Laura Li, Ph.D. of BT Genomics, and Dr. Allan Feingold

- Instead of filing a response brief or evidence, plaintiff's counsel (Maune Raichle) stipulated to WGS and initial reporting of results for over 400 genes

- Initial results to be reported include all 81 genes listed in Tables 2 and 3 in Belcaid 2023, a review of reviews listing genes known to have been found to carry germline mutations in people with mesothelioma

- Judge Viscomi so ordered the stipulation but noted:
  - *The court has approved the stipulation reached by the parties, but this should not be interpreted as the court taking any position on the issue being litigated.*

WGS and Flexible Sequencing Utilized

- During the winter, blood draw and WGS took place
- Flexible DNA sequencing results reporting took place
  - results are not public
- Dr. van Zyl timely filed his report in January 2025
- Plaintiff did not file a report by deadline and did not file a motion to extend time
- Current schedule calls for:
  - expert deps to be done by late June
  - Daubert hearings completed in September
  - October 6 - trial starts

Notable Recent Genetic Testing Ruling

March 10, 2025 Genetic Testing Ruling - Combs – Alameda

- Attention should be given to recent proceedings before Judge Patrick McKinney in the Combs case in Alameda County; *23CV056760: COMBS, et al. vs ABB INC., et al.*

- Contra Costa and other defendants moved for sequencing of 28 genes, relying on a declaration by Dr. Lewis A. Chodosh and the genes listed in a mesothelioma-specific gene panel offered by the University of Chicago

- Plaintiff opposed sequencing of genes other than *BAP1; p*laintiff relied on a declaration by Dr. Wayne W. Grody

- The experts were **not** deposed.

More re Genetic Testing Ruling - Combs

- Judge McKinney heard oral argument after issuing a 2/5/25 tentative order limiting sequencing to BAP1; the argument transcript deserves review
- Ultimately, Judge McKinney issued a 2/10/25 order which mainly retained the tentative order, but at page 2 also included language allowing additional expert testimony:

> "At the hearing, all counsel seemed to understand that this was cutting edge medical research; and that evidence of a plausible causal link between a germline mutation of BARD1, for instance, and mesothelioma may be discovered in the coming years. Recognizing that these developments might happen while this case is pending, the Court permits Defendants to renew their motion to compel genetic testing of germline mutation of one of the identified genes if and only if a qualified individual can testify that additional cancer research has demonstrated a plausible causal link between the identified germline mutation and mesothelioma unrelated to exposure to asbestos."

More re Genetic Testing Ruling - Combs

- Contra Costa and plaintiff did **not** submit additional expert testimony
- In many ways, the declarations were 2 ships passing in the night as they addressed different aspects of genomics
- Both declarations did not mention Dr. Testa's 2022 concessions in Watts that 1) genetic abnormalities can cause mesotheliomas, and 2) mutations in a particular person are unpredictable
- Both declarations also did not cover key recent studies on genomic causation, such as:

1) Congedo 2024 (estimating genetic causation of 20% of mesotheliomas)
2) Febres-Aldana 2024 (MSK researchers acknowledge genetic causes of mesothelioma)
3) Nielsen 2025 (Dr. van Zyl's 2025 study showing over 90% Bayesian certainty that a single null variant BAP1 mutation can initiate and drive mesotheliomas and other cancers)

More re Genetic Testing Ruling - Combs

- Contra Costa took a writ seeking interlocutory review; the submission was comprehensive, including the declarations and transcript of oral argument; see First District docket # A172581
  - https://appellatecases.courtinfo.ca.gov/search/case/disposition.cfm?dist=1&doc_id=3124683&doc_no=A172581&request_token=OCIwLSEnTkw8WzBRSCI9WEtIUFw6UVxfJCI%2BUzJTLDtOCg%3D%3D

- Intermediate appellate court summarily denied the writ request; Contra Costa has a pending request for review by the California Supreme Court – see docket S289786

- Writ papers include hearing transcript, expert declarations, and motion papers
  - https://www.dropbox.com/scl/fo/btg9ywa79hb3ova1zx880/ALYFlqAFBPBYkkB39IhWa1M?rlkey=ji0rdtlp8750in82sjsd997rs&e=1&dl=0

Flexible Sequencing

Flexible Reporting of Sequencing Results Reduces Inefficiencies and Disputes

- Disputes over the scope of and reporting of sequencing results really should not arise because Dr. Testa and others have proved and testified that it is not possible to predict which genes carry germline mutations or which mutations are present
  - nonetheless, time wasting and economically inefficient disputes sometimes are generated by lawyers

- To reduce disputes and waste, we worked with a small CLIA certified sequencing lab in California to develop a flexible sequencing results reporting process

- To avoid wastes of time and/or money for litigants and courts, the lab will run whole genome sequencing (WGS) so that the best possible and complete sequencing data is captured and stored

- The lab, however, is smart and flexible, and so will initially report sequencing results only for the set of genes agreed to by the parties or ordered by a judge

- Subsequently, the lab will report additional sequencing results if agreed to by the parties or ordered by a judge

Genomic Evidence

Genomic Evidence is Admissible and Can Be Dispositive

- Contrary to the claims of some lawyers, genetic evidence has been admitted in court on disease causation
- In fact, some courts have entered summary judgment orders for defendants based on the strength of genetic evidence
- Those orders include the seminal 2006 case in which summary judgment was entered for the defense after genetic testing established that terrible malformations of children were caused by a genetic mutation that causes CHARGE syndrome rather than exposure to a fungicide, *Bowen v. E.I. DuPont de Nemours & Co.*, 906 A.2d 787 (2006)
- Another example is *Ortega v. United States*, 2021 U.S. Dist. LEXIS 188969, 2021 WL 4477896 ("Because all evidence in the record indicates that J.A.O.'s neuromuscular failure was caused by a congenital [genetic] condition rather than by negligence on the part of the healthcare providers, both motions [for summary judgment] are granted.")

Granillo - Plaintiff's MIL re ALK Gene Fusion

- Granillo case is set for trial this spring, and involves a mesothelioma in a woman under 30; # 22 STCV 14155 – Los Angeles

- In general, several experts retained by defendants opined mesothelioma was caused by an *ALK* fusion which arose from genomic instability induced by *BRCA1* mutation, citing 21 case reports

- Maune firm MIL #4 argues that defense expert opinions should all be excluded as speculation because there are no epidemiologic studies of women with pathogenic *BRCA1* mutations, *ALK* fusions and mesothelioma

Granillo - Plaintiff's MIL re ALK Gene Fusion

- Per Maune Raichle motion, 21 case reports are not enough:
  - "B. The Proffered Opinions, Based Solely on Case Reports of Approximately 21 Individuals World-Wide is Marginally Probative but Will Greatly Confuse the Jury and Ev. C. 352 Requires Exclusion"
- Defendants could be arguing that plaintiff firms that oppose genetic testing are in essence involved in spoliation by destroying/blocking the gathering of evidence
- Citing Maune Raichle's MIL, defendants also could be arguing that plaintiff courts are depriving defendants of due process if they 1) block whole genome sequencing and 2) block experts from re-using genetic data in multiple cases

Plaintiff Tactic – Ignore Data and Focus on Words Not In the Article

- Scientific studies are based on data
  - "In God we trust, all others must bring data"
    - Generally attributed to W. Edwards Demming
    - https://www.ibm.com/think/insights/in-god-we-trust-all-others-must-bring-data#:~:text=%E2%80%9DIn%20God%20we%20trust.,data%20analysis%20is%20equally%20important

- Regarding genomic findings, plaintiff tactics often appear to focus on ignoring data and instead focusing on words not in an article

Challenges to Differential Etiology

- Granillo plaintiff MIL#4 and defense motions illustrate challenges to etiology opinions

- Plaintiff's can challenge opinions of defendant retained experts who state conclusions but are not expert in genetics
- Defendants can challenge the scientific reliability of an etiology opinion rendered by a witness (e.g. Drs. Kradin and Zhang) who automatically attributes causation to a known or unknown exposure to a toxicant such as asbestos

- For genetics in particular, experts may be excludable due to:
  - failure to actually analyze recent scientific literature
  - failure to actually analyze the cancer syndrome significance of a personal or familial history of cancers or other non-cancer diseases/conditions
  - failure to utilize reliable, reproducible methods and data, including calculation of CADD scores, assessment of Hallmarks of cancer, and assessment of VAF %s

Dr. Kradin Excluded for Failure to Address Alternative Causes

- Keller v. Exxonmobil Oil Corp., 2025 U.S. Dist. LEXIS 44043
  - https://asbestoscasetracker.com/summary-judgment/defendants-motionfor-summary-judgment-granted-based-on-expert-preclusion/Text
- "Dr. Kradin's subsequent deposition testimony regarding his skepticism about radon (Kradin Tr. at 26-27) may have merit, but this post hoc rationale, which is not in any way memorialized in his report, does not indicate that the methods he previously employed to form the opinions contained in the report were reliable. (Id. at 25 ("A. I didn't look at any other contributing factors [other than asbestos and secondhand smoke]. Q. Were you asked to look at radon? A. I wasn't asked to look at radon.")); see also, e.g., Wills, 379 F.3d at 45-46 (finding that expert's failure to account [*24] for smoking and alcohol habits in reaching conclusions regarding cancer causation, despite concession that they were major risk factors, indicated that the conclusions were "not grounded in reliable scientific methods").

Common Genomic Mistakes to Avoid

- Classification of a mutation as a VUS (variant of unknown significance)
  - is not gospel; classifications change
    - Waters 2024 changed classification for many for *BAP1* mutations
  - does not mean the mutation is benign

- "Paper" sequencing reports often exclude huge amounts of data; obtain digital data

- Reports about "actionable" mutations are not complete

- Two benign mutations can be lethal if located "in cis"

"Benign" Variants May Not Be Benign – *BARD1* example

- Novelli *et al*. 2024: rare heterozygous pathogenic germline variants in the (*BARD1*) gene cause malignant mesothelioma, particularly in young patients with no known history of asbestos exposure

- Li et al (2021) reported the discovery of two *BARD1* mutations, namely p.Pro24Ser and p.Arg378Ser, simultaneously in patients of a hereditary breast and ovarian cancer family.

- *"These BARD1 mutations, in isolation, cause no readily obvious phenotype*; *but when combined in cis, they dramatically impaired the DNA Damage Response (DDR) pathways leading to rapid genome wide instability in affected cells, resulting in tumors in vitro and in vivo*."

- *Cis* effects are caused by genetic variants located on the same DNA molecule

- Neither of the single mutations causes a functional change, but together they synergistically impair the DNA damage response and lead to tumors *in vitro* and *in vivo*.

BAP1

BAP1 Update and Limits of Sequencing Methods

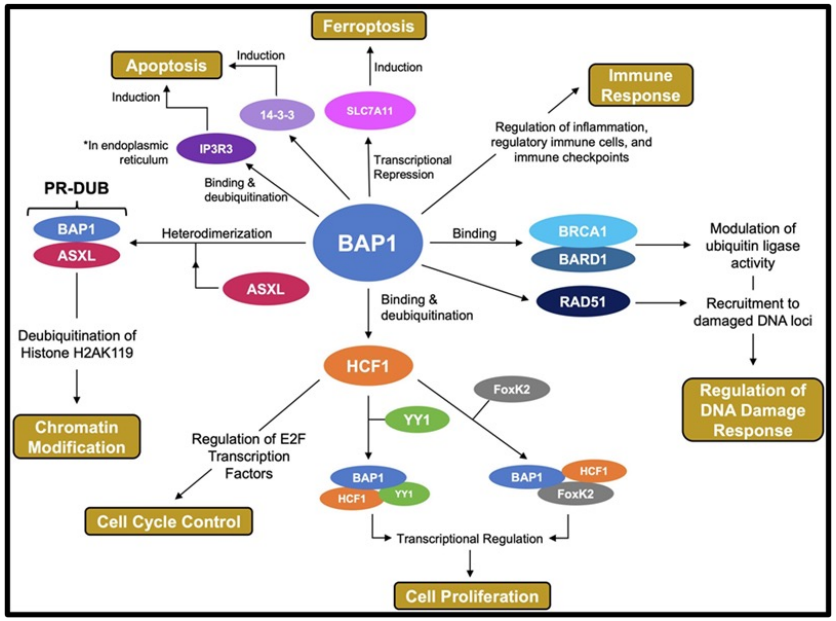
- All stakeholders need to understand Nielsen 2025, the recent study by Dr. van Zyl and colleagues

- In Cowger, Combs and other cases, plaintiffs explicitly or implicitly conceded to DNA sequencing of BAP1

- Stakeholders need to understand that sequencing methods are **not** fungible; WGS provides the most scientific certainty
  - exome sequencing of BAP1 is **not** dispositive of whether a mutation is present because exome sequencing omits about 98% of each gene and has other flaws

Proteins Interact – One Mutation Can Impair the Function of Many Proteins

- BAP1 stands for **BRCA1-Associated Protein 1 (BAP1)**
- BAP1 protein interacts with many other proteins
- TP53 protein interacts with even more proteins



Adapted from Louie and Kurzrock, 2020

BRCA1 and 2, BARD1 and Others

Recent Evidence on Germline Mutations in Non-Smokers, Including Germline BRCA1 and 2

- Germline mutations of BRCA1 and 2 are pertinent to more than breast cancer and ovarian
- Germline mutations of BRCA1 and 2 also can cause lung cancers, mesotheliomas, prostate cancers, pancreatic cancers and
  - Carapezza G, Minardi SP, Noci S, et al. Germline Whole-Exome Sequencing in Non-Smoker Lung Cancer Patients Reveals Pathogenic Variants in Lung Cancer Driver Genes. Genes Chromosomes Cancer. 2025;64(3):e70040.

ABSTRACT

- "Approximately 10%–15% of all lung cancers arise in non-smokers."
- "Seven of the genes we identified (54%) are involved in DNA repair (ATM, BRCA1, BRCA2, FH, MLH1, MUTYH, and TP53) [26] suggesting that variants in this pathway may cause deregulation of DNA repair and cell cycle and increase cancer risk."
- "Whole-exome sequencing was performed on genomic DNA from peripheral blood Overall, our results strongly support the concept that non-smokers lung cancer patients carry PGVs [pathogenic germline variants] in cancer predisposing genes, especially in lung cancer driver genes, and are directly and/or indirectly involved in cancer development."

Some BRCA1 and 2 Germline Mutations Make Smoking and Drinking Relevant to Mesos

- Contrary to conventional wisdom, smoking has always been relevant to mesothelioma, as previously pointed out by Dr. Moolgvakar in Dr. Testa's book on mesothelioma; epidemiologists missed the effects for various reasons
- Dr. van Zyl's slides quote studies that explain that aldehydes cause endogenous genomic abnormalities
- Aldehydes arise from many sources, including smoking and drinking

More re Aldehydes and Cancers

- Aldehydes can have even stronger effects in people with pathogenic *BRCA1* and 2 mutations and Type 2 diabetics by degrading protein from a normal copy of a gene
- Same mechanisms at work for cancers attached to many organs
- Same mechanisms may well be at work with mutations of other genes

Learn Endogenous Mechanisms

- Dr. van Zyl's slides show multiple endogenous (internal) mechanisms that cause cancers

- Stakeholders need to really understand these mechanisms because they explain why some cancers arise independent of external exposures

"2 Hit" Theory Has Many Exceptions

- Dr. van Zyl's slides show an example of endogenous mechanisms can cause exceptions to "2 hit theory"
- Stakeholders need to really understand the exceptions to 2 hit theory
- "Tissue specific" haploinsufficiency is an important concept
- Many TSG's can act in a haploinsufficient manner for tissue specific reasons

Dr. Moline Ordered to Turn Over Names of People Who Were Utilized in Studies

- Prior experiences have shown that Dr. Moline's etiologies often fail to meaningfully address personal and family histories of cancers and other diseases

- Per a recent order by Judge Silvera (key quote below), April 8 is the date for Dr. Moline to turn over the records identifying the people who were the subjects of her "studies."
  - Johnson & Johnson v. Northwell Health Inc, 2025 N.Y. Misc. LEXIS 1839

    - "Nonetheless, in light of the Court of Appeals' decision denying Northwell's motion for leave to reargue its motion for leave to appeal, see NYSCEF Doc. No. 125, this Court orders Northwell and Dr. Moline to comply with the First Department's Decision by turning over the documents requested in the Subpoenas by April 8, 2025."

- Stakeholders will need to investigate and understand cancer and other histories from subjects of studies

Reminders

Genetic Testing Results Are Often in Medical Records

The Plaintiff Did Not Timely Produce Genetic Testing Results in Both Mizer and Kudenov Cases

- Despite the frequent presence of genetic testing results in medical records for people with mesothelioma, the plaintiff did not timely produce genetic testing results in both the Mizer and Kudenov cases

- In Mizer, in August 2024, plaintiff's counsel (Maune Raichle) belatedly produced a Foundation Medicine genetic testing report dated May 2023
  - The report revealed, among others, the presence of a pathogenic *BAP1* mutation

- In Kudenov, in September 2024 (essentially at the start of trial), plaintiff's counsel belated produced a Foundation Medicine genetic testing report dated in February 2024
  - The report revealed, among others, the presence of a pathogenic *ERCC4* mutation

Whole Genome Sequencing Usually is Key

Exome Tumor Sequencing Misses About 98% of Each Gene, and Does Not Rule Out Other Mutations

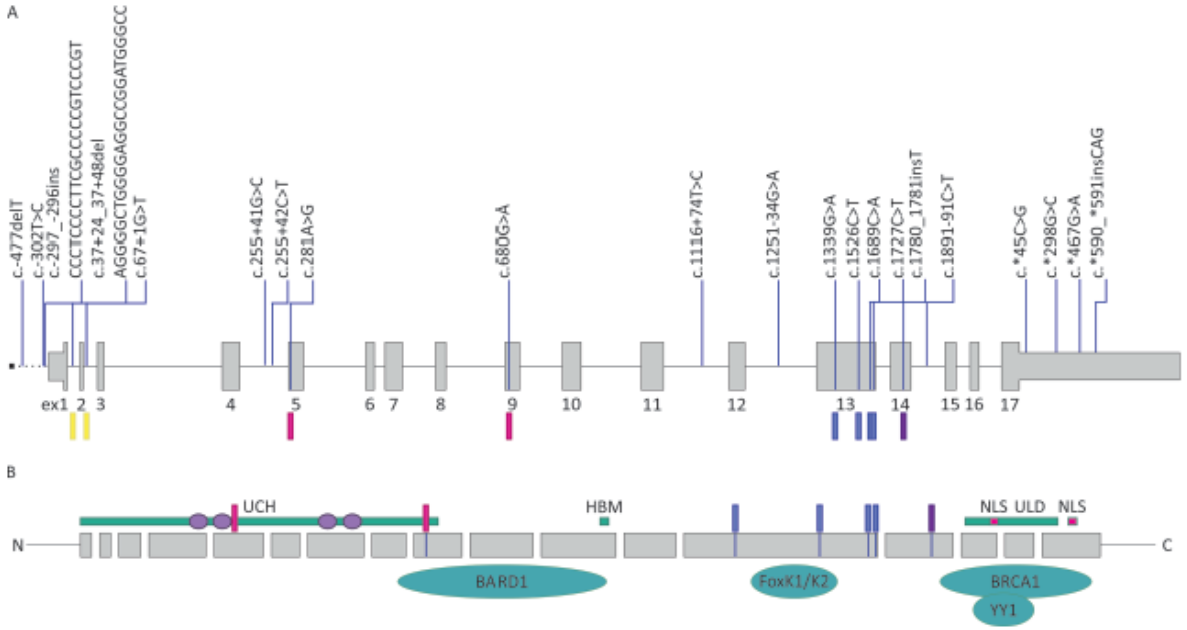
- Exome sequencing gene "panels" have inherent limitations:
  - they do no detect variants in deep intronic regions of genes, and do not detect large deletions, whole gene deletions, and large structural rearrangements.

- Somatic tumor sequencing does not rule out the possibility that a person carries pathogenic germline mutations

- These principles actually matter for mass tort cases
  - For example, multiple published peer reviewed studies have now shown that familial whole *BAP1* gene deletions do occur, including deletions of large sections of the *BAP1* gene (*i.e.*, Walpole *et al.*, 2018; Boru *et al.*, 2019; Carbone *et al.*, 2022; Pandithan *et al.*, 2022 etc.)

Pathogenic Mutations Exist in Intronic and Other "Regulatory" Regions

- Similarly, multiple peer reviewed published studies have also highlighted the importance of screening deep intronic regions of *BAP1* gene for pathogenic mutations (i.e., Repo *et al.*, 2019; Ohar *et al.*, 2016 etc.)



Adapted from Repo *et al.*, 2019

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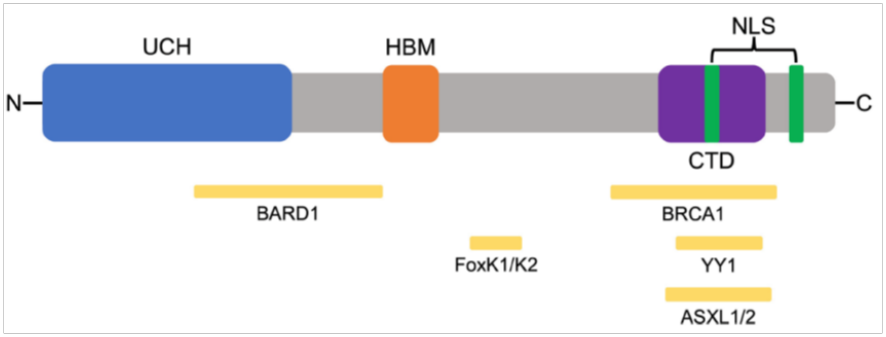
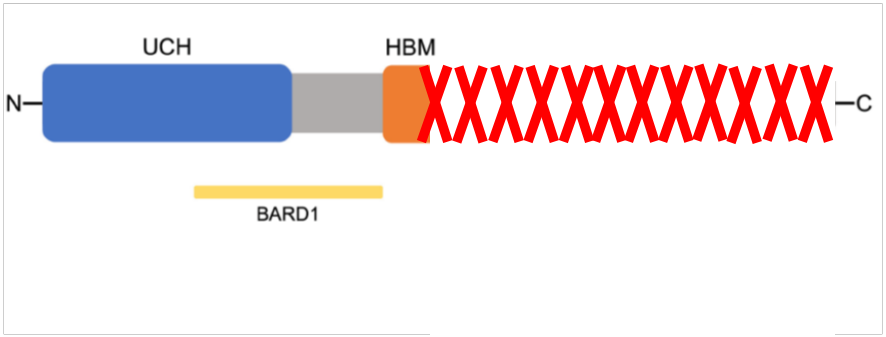
Specifics Matter : Pathogenic *BAP1* p.Arg385Ter - A Truncating Null (Loss-of-Function) Germline Mutation

Wild Type (Normal) BAP1 Protein Structure (729 amino acids)



The Germline *BAP1* p.Arg385Ter null mutation truncates (terminates) the BAP1 protein at amino acid 385, resulting in a BAP1 (1-385) mutant protein that lacks more than half (53%) of its coding region. The BAP1 protein encoded by this mutant gene is incapable of carrying out normal *BAP1* functions.



https://www.ncbi.nlm.nih.gov/clinvar/variation/485271/

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“Genetic Defenses” are Not All the Same

"Genetic Defenses" are Not All the Same

- Some stakeholders incorrectly argue as if all "genetic causation defenses" are the same
- In fact, the extent and power of a genetic causation defense depends on multiple factors
- Generally speaking, "genetic causation defenses" can and do fall into multiple different "buckets" with different sets of supporting evidence

"Replication Error" Defense

- For example, a "replication error" genetic defense has relatively little factual focus on the particular plaintiff
- A "replication error" defense is based mainly on the general principles that 1) pathogenic mutations can and do occur when cells divide themselves (mitosis) in order to produce new cells (replication), and 2) some replication error mutations that were not repaired may cause a cancer
  - to oversimplify, some key aspects of this defense are based on the so-called "bad luck" studies by Drs. Vogelstein, Tomasetti and others
- To the best of my knowledge, all "genetic causation defense" mesothelioma trials that have gone to verdict have been "replication error" defenses, sometimes with some additional facts unique to the plaintiff

Defense Based on Plaintiff Specific Mutations

- In contrast, other "genetic causation defenses" are based on the results of genetic sequencing results specific to the plaintiff, often including personal and familial medical histories of cancers and/or other conditions
  - Key aspects of this defense are based on results of germline sequencing and/or somatic sequencing (tumor sequencing)
  - Additional aspects involve application of reliable, reproducible methods and date, including calculation and presentation of CADD scores and VAF %s

- To the best of my knowledge, no one has tried such a case to verdict

- I can say with certainty that no one has tried to verdict a case in which Dr. Len van Zyl has been called to testify

CADD Scores

CADD Scores Can Play a Significant Role in Differentiation Between Disease Causing and Benign Gene Variants

- CADD analysis provides an objective, quantitative method of assessing likely pathogenicity of gene variants (mutations) (Kircher *et al.*, 2014; Rentzsch *et al.*, 2019; 2021).
- CADD scores are especially useful when functional empirical evidence is lacking or insufficient to make an evidence-based determination.
- CADD integrates over 60 existing commonly used predictive algorithm tools, each with their own criteria and inherent biases (Kircher *et al.*, 2014; Rentzsch *et al.*, 2019; 2021).
- The resulting CADD score provides an objective, quantitative metric of deleteriousness/pathogenicity to better guide the treatment options and research directions available to clinicians and researchers (Kircher *et al.*, 2014; Rentzsch *et al.*, 2019; 2021).

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General Meaning of CADD Scores

- **A CADD score of 15 is the recommended minimum cutoff to identify deleterious mutations** (Kircher *et al.*, 2014; Rentzsch *et al.*, 2019; 2021).
- **A CADD score of 20 indicates that a variant is among the top 1% of the most deleterious variants in the human genome** (Kircher *et al.*, 2014; Pastorino *et al.*, 2018).
- **A CADD score of 30 places a variant in the top 0.1% of the most deleterious variants (mutations) in the human genome** (Kircher *et al.*, 2014; Rentzsch *et al.*, 2019; 2021).

CADD Scores for Gene Variants in Mesothelioma Research Studies (Dr. Testa - Cheung *et al.*, 2021)

Table 2. Variants observed in germline DNA from 14 MM patients

Patient	Gene(s)	Variant(s)	Predicted Protein Change(s)	Type of variant(s)	ExAC_All %; CADD score
ABS2406	*MSH4*	NM_002440.4:c.719dupT	NP_002431.2:p.Ile240fs	Indel	Novel; 35
ABS2640	*CHEK2*	NM_007194:c.909-2028_1095+330del5395	NP_009125.1:p.M304Lfs*16	Del. (exons 9-10)	Novel; NA
	DACT2	NM_214462.3:c.533C>T	NP_999627.2:p.Ser178Leu	Missense	Novel; 25.9
	LRRK2	NM_198578.3:c.6055G>A	NP_940980.3:p.Gly2019Ser	Missense	0.0004; 32
ABS2813	*MUTYH*	NM_001128425.1:c.389-1G>A	Frameshift / truncation	Splice site	Novel; 33
ABS3425	*DNMT3A*	NM_022552.4:c.2631delC	NP_072046.2:p.Ser689fs	Indel	Novel; 35
	POLE4	Whole gene deletion	No protein expression	Whole gene del.	Novel; NA
	APC	NM_000038.5:c.1642T>G	NP_000029.2:p.Leu548Val	Missense	Novel; 22.7
ABS3460	*POLQ*	NM_199420.4:c.3589C>T	NP_955452.3:p.Arg1197*	Nonsense	1.65E-05; 35
	XRCC1	NM_006297.2:c.175delG	NP_006288.2:p.Asp59fs	Indel	8.24E-06; 35
	SETD1B	NM_015048.1:c.2554C>T	NP_055863.1:p.Arg852Cys	Missense	5.11E-05; 24
	ARID1B	NM_017519.2:c.2405C>T	NP_059989.2:p.Ser802Leu	Missense	0.0004; 32
946-P	*BRCA2*	NM_000059.3:c.657_658del	NP_000050.2:p.Thr219fs	Indel	6.12E-05; 22
	LRRK2	NM_198578.3:c.5314_5317+6delAAAGGTAAGG	Frameshift/truncation	Indel at splice site	Novel; 35
R88-T	*LRRK2*	NM_198578.3:c.5314_5317+6delAAAGGTAAGG	Frameshift/truncation	Indel at splice site	Novel; 35
	ATM	NM_000051.4:c.1837G>T	NP_000042.3:p.Val613Leu	Missense	4.26E-05; 25.5
ABS3383	*CHEK2*	NM_007194:c. 1451C>T	NP_009125.1:p.Pro484Leu	Missense	0.0001; 29.7
	POLE	NM_006231.2:c.177G>C	NP_006222.2:p.Lys59Asn	Missense	4.12E-05; 21.7
ABS3481	*ATR*	NM_001184.4:c.4351C>T	NP_001175.2:p.Arg1451Trp	Missense	0.0003; 26
	JARID2	NM_004973.4:c.3682G>A	NP_004964.2:p.Val1228Met	Missense	6.59E-05; 23.7
ABS3505	*POLQ*	NM_199420.4:c7024_7026TAA>AAT	NP_955452.3:p.Leu2342Ile	Missense	0.0002; 24.2
	BRIP1	NM_032043.3:c.2220G>T	NP_114432.2:p.Gln740His	Missense	0.0005; 23.7
	CBFA2T3	NM_005187.5:c.956G>A	NP_005178.4:p.Cys319Tyr	Missense	1.76E-05; 23.7
	RHBDF2	NM_024599.5:c.1726A>G	NP_078875.4:p.Ile576Val	Missense	2.02E-05; 21.6
ABS3572	*MLH3*	NM_001040108.2:c.G3455G>A	NP_001035197.1:p.Arg1152His	Missense	6.59E-05; 24.1

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Multidisciplinary group of geneticists, scientific consultants, and counsel offering consulting and expert services in genomics & systems biology regarding toxins

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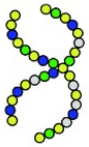

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